Phase I Adoptive Cellular Therapy Trial with Endogenous CD8+ T Cells (ACTolog® IMA101) in Patients with Relapsed and/or Refractory Solid Tumors

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Background, Study Objectives, and Methods

Background

- Adoptive cellular therapy (ACT) for solid tumors is challenging due to lack of targets with high tumor specificity and disease recurrence associated with loss of single antigen expression.
- ACTolog® (IMA101) is a fully personalized multi-target ACT approach designed to overcome these limitations by generating autologous T-cell products that are redirected towards multiple novel tumor targets identified by Immatics' proprietary XPRESIDENT® technology platform. Within this personalized approach, tumors positive for >1 target of a predefined target warehouse are identified and tumor-specific T-cell products directed against up to 4 targets are manufactured for individual patients.
- We initiated a phase I study using 8 target antigens (ACTolog® warehouse), which are highly expressed across tumor types and minimally expressed in normal tissues.

Study Objectives

- **Primary:** To evaluate the safety and tolerability of IMA101 alone (Cohort 1) or in combination with atezolizumab (Cohort 2)
- **Secondary:** To evaluate i) feasibility of the ACTolog® manufacturing process; ii) *in vivo* persistence and *ex vivo* functionality of transferred T cells; iii) rates of tumor response rate, and response duration of IMA101 alone (Cohort 1) or in combination with atezolizumab (Cohort 2); iv) feasibility of the *in vitro* diagnostic device IMADETECT™; and v) tumor and blood biomarkers (e.g. target expression analysis; T-cell infiltration in the tumor, T-cell precursor analysis).

Methods

- Evaluation of expression of HLA-A*02:01 restricted targets in the ACTolog® warehouse using the *in vitro* diagnostic device IMADETECT™ (qPCR assay) (Fig. 1).
- Persistence of adoptively transferred target-specific CD8 T cells was determined by multimer staining.
- ACTolog® treatment: lymphodepletion (fludarabine/cyclophosphamide) is followed by IMA101 infusion of up to 4 antigen-specific T-cell products and s.c. low-dose IL-2 (up to 7 doses). Atezolizumab is given to patients enrolled on cohort 2, ≥ 3 weeks post IMA101 infusion, upon hematologic recovery (www.clinicaltrials.gov NCT02876510).

Figure 1. ACTolog®: Treatment Algorithm

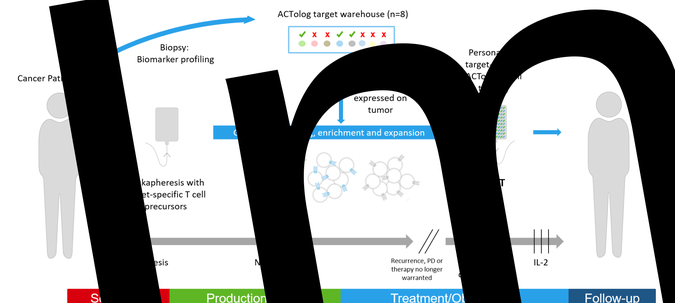

Table 1. nt Screeni d Treatment St

Screening/Treat us	No. of Patients
Screened	200
HLA-A*02:01-posi	87 (43.5%)
Tumor biopsy	51
Leukapheresis	36
Completed treatment	9
Patients who had tumor biopsy, but no leukapheresis	No. of Patients
Biopsy negative for ≥1 target	6
Worsening performance status	2
Insufficient tumor tissue	2
Inadequate pulmonary function tests	1
On other therapy	4

Table 2. Pa st and ACT nfusion Data

Patient No.		Tumor Type	Previous Treatments	Disease Site	Years	Expression	Pr	Total Viable Cells Infused
1		Hormone-receptor positive, HER2-negative breast cancer	Sur Tamox Doxor ycin, Cyclophosphamide, Pac le, Paclitaxel, Capecitabine, L dronic acid, Gemcitabine, Nav trozole, Palbociclib	Pleura, liver, ilium, calvarium, lung, node	18	Ag012-01 Ag016-02	Ag0	24 x 10⁹
2		Synovial sarcoma	Su tion, Doxorubicin, Ifosfamide, Durvalu limumab, Pazopanib, Olaratu	eural and subp odules, parasp enhancing mas	10	Ag008-01 Ag012-01 Ag016-02	16-0 Ag018-01	10¹⁰
3		Myxoid liposarcoma	Surg on, Doxorubicin, Ifosfamide, Gemcitab tedin, Adriamycin, Dacarbazin n, AKT inhibitor	cipital bone, rena d retroperitoneal space		01 Ag012-01 Ag018-01	Ag008-01 Ag012-01 Ag018-01	1.16 x10¹⁰ 1.16 x 10¹⁰ 1.16 x 10¹⁰
4	3 (M)	opharyngeal arcinoma	Surgery, Paclitaxe Cisplatin, Taxane, Cetuximab, , Carboplatin, Gemcitabine, U, Atezolizumab	Right neck (encasing common carotid artery)	12	Ag012-01 Ag013-01	Ag012-01	1.69 x 10¹⁰
5	58 (M)	amous cell oma of the anus	Surgery, Radiation, Carboplatin, Paclitaxel, 5-FU/Cetuximab, Atezolizumab and Bevacizumab, OX40+TLR4 inhibitors	Lung, liver, peritoneal cavity	4	Ag008-01 Ag012-01	Ag008-01 Ag012-01	9.69 x 10⁹ 7.62 x 10⁹
6*	32 (F)	Hormone receptor-negative, HER2-positive breast cancer	Surgery, Radiation, Adriamycin, Cyclophosphamide, Docetaxel, Herceptin, Pertuzumab, Goserelin, Exemestane, Trastuzumab emtamsine, Lapatinib/Capecitabine, Trastuzumab, Everolimus, Letrozole	Supraclavicular fossa metastasis, lymph node	3	Ag012-01 Ag008-01 Ag013-01	Ag012-01 Ag008-01	1.61 x 10¹⁰ 3.33 x 10⁹
7*	49 (F)	Synovial sarcoma	Surgery, Radiation, Adriamycin, Ifosfamide, Pazopanib, IDO Inhibitor	Lung, pleural, pancreas, right perirectal space	4	Ag008-01 Ag012-01 Ag016-01	Ag008-01 Ag012-01 Ag016-01	1.74 x 10¹⁰ 9.08 x 10⁹ 1.32 x 10¹⁰
8*	25 (F)	Ovarian cancer	Surgery, Carboplatin, paclitaxel, Adriamycin, Cytoxan, Letrozole, Cisplatin, Gemcitabine; Surgery	Peritoneal cavity, midline cul-de-sac, lymph node	2	Ag012-01 Ag013-01 Ag016-02	Ag012-01 Ag013-01 Ag016-02	1.16 x 10¹⁰ 1.41 x 10¹⁰ 1.16 x 10¹⁰
9*	25 (F)	Triple-negative breast cancer	Adriamycin, Cyclophosphamide, Paclitaxel; Surgery; Radiation; Capecitabine; Surgery; Eribulin	Mediastinum lymph nodes, lung, Pleura	3	Ag012-01 Ag018-01	Ag012-01 Ag018-01	1.04 x 10¹⁰ 1.74 x 10¹⁰

*Cohort 2

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Results and Conclusions

Results

- From July July 2017 to July 2019, 200 patients were screened. Nine patients were tr date. The median number of prior therapies was 6 (range 3 to 12).
- The most common adverse events (grade ≥ 3) were cytopenia caused by lymphodep able 3) and grade 1-2 cytokine release syndrome (8 of 9 patients).
- Eight patients had restaging imaging data (9th patient , too early for response assessment). All 8 patients had stable disease by RECIST and irRECIST at 6 weeks, includin oma of the anus who had reduction in tumor measurements by 2 Y RECIST and irRECIST). All 8 patients are alive to date after up of 194 days (ran 56).
- One patient (#4) entered study with progressive disease after 12 f therapies; has required no further treatment 10 month dications and o work (persistence data, Fig. 2a).
- Infused T-cells show excellent persistence with high frequen up to 12 weeks after infusion for the first eight p nts . Figu the media equency of target-specific CD8 T cells .

Conclusions

- ACTolog® IMA101 is safe and well-tolerated. No seriou
- All patients had stable d eeks after T-cell th
- Initial T-cell p ed high prevalence a xpected T-cell pher hich are imp erequisites for clinical activity.
- Overall, I consistent with t n ACT safety profile considered ble for the patients with advanced metastatic cancer refractory to standard t
- The tri ng.

re 2. T-Cell tence in ted Patients

a. t #4 (Nasopharyn cer) with a et **b. Persiste doptively t CD8 T cells**

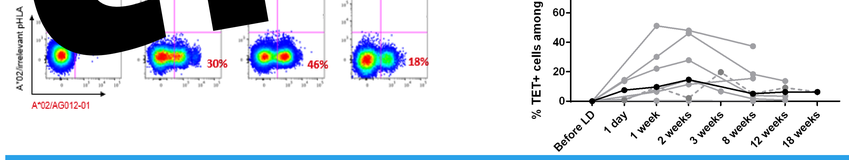

Table 3. Safety Profile for Enrolled Patients

Adverse Events	≥ Grade 3 (n)*	SAE (n)	AESI (n)
Anemia	7	0	0
Leukopenia	5	0	0
Lymphopenia	5	0	0
Neutropenia	6	0	0
Thrombocytopenia	3	0	0
Bacteremia**	1	1	0
Cellulitis**	2	2	0
Abdominal infection**	1	1	0
Port-related infection	1	0	0
Sinus bradycardia**	1	0	1
Cytokine release syndrome	0	0	8
Infusion-related reaction	0	0	1

Abbreviations:
SAE, serious adverse event;
AESI, adverse event of special interest

* If a pt. experienced > 1 event, the pt. is counted only once for the most severe AE.
* * If an AE was ≥ grade 3 AE, the same AE was also counted for either SAE or AESI.